AMENDMENT UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1646

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Turner, Jr. and Mathur

Group Art Unit: 1646

Application No.: 09/714,883

Examiner: O. Chernyshev

Filed: 11/16/2000

Atty. Dkt. No.: LEX-0092-USA

Title: Novel Human Secreted Proteins and Polynucleotides Encoding the Same

RESPONSE TO OFFICE ACTION DATED FEBRUARY 19, 2002

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The Applicants acknowledge the receipt of the Office Action ("the Action") mailed on February 19, 2002 (Paper No. 9), which has been carefully reviewed and studied. Reexamination and reconsideration of the application is requested in view of the following remarks. In order to facilitate the Examiner's evaluation of the application, Applicants have attempted to address the rejections in Paper No. 9 in the same order in which they were originally raised.

This response is believed to be timely filed. Applicants believe no fees are due in connection with this response. However, the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

RESPONSE

I. Status of the Claims

No claims have been canceled, amended or added.

Claims 1-3 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**.

II. Rejection of Claims 1-3 Under 35 U.S.C. § 101

The Action first rejects claims 1-3 under 35 U.S.C. § 101, as allegedly being drawn to an invention with no apparent specific and substantial credible utility. Applicants respectfully traverse.

As discussed in Applicants response to the previous Office Action mailed July 9, 2001 ("the previous Action"), the Examiner seems to be requiring data "which associates the instant DNA or encoded protein with any diseases or disorder" or that shows the "use of the protein as a marker for any disease or condition" (the previous Action at page 4). This is reiterated in the present Action, with the Examiner stating that the "instant claims are drawn to a DNA and the protein encoded thereby of as yet undetermined function or biological significance" (Action at page 2).

Applicants would like to invite the Examiner's attention to the fact that sequences sharing 57% percent identity at the protein level with the described sequence are present in the leading scientific repository for biological sequence data (GENBANK), and have been annotated by third party scientists *wholly unaffiliated with Applicants* as "human ceruloplasmin" (GenBank accession number M13699) and "homo sapiens ceruloplasmin (GenBank accession number NM_000096). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given these GenBank annotations, there can be no question that those skilled in the art would clearly believe that Applicants' sequence is a ceruloplasmin.

Additionally, with regard to the Examiner's statement in the previous Action that there is no data "which associates the instant DNA or encoded protein with any diseases or disorder" or that shows the "use of the protein as a marker for any disease or condition" (the previous Action at page 4), Applicants point out for the record that the association between ceruloplasmin and Wilson's disease

was discussed in the present application, at least at page 12, lines 1-2, and, further, that this relationship between ceruloplasmin and Wilson's disease has long been recognized by skilled artisans, as evidenced by a steady stream of scientific manuscripts describing the relationship between Wilson's disease and ceruloplasmin, with the first such manuscripts published as early as 1965, and the description of this relationship in well over 100 scientific manuscripts. Thus, ceruloplasmins, such as the presently described protein, have a well-established utility, as the relationship between Wilson's disease and ceruloplasmin is very well-known in the art. Additionally, it is known that different ceruloplasmin isoforms serve as an accurate marker for Wilson's disease (for example, see Chowrimootoo *et al.*, 1998, Arch. Dis. Child Fetal Neonatal Ed. 79:F198-201). Thus, the skilled artisan would readily appreciate the utility associated with the provision of novel human sequences related to ceruloplasmin, and therefore, the present utility rejection must fail.

The Examiner states that "(t)he protein of the instant invention does not belong to a family of compounds with a common, well established specific and substantial utility" (Action at page 3). However, the evidence provided herewith conclusively establishes that this is clearly not the case. Thus, Applicants reliance on *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") in the response to the previous Action is not at all misplaced. In *Brana*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context

> of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

As discussed in the response to the previous Action, the specification teaches that the present nucleotide sequence encodes a human ceruloplasmin, and that ceruloplasmins are associated with many human diseases, including Wilson's disease. Furthermore, the described sequence provides a specific marker of the human genome, and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips. Accordingly, as opposed to the contention in the Action that "any nucleic acid encoding a protein, which is differentially expressed, can be employed in a DNA chip for assessing gene expression patterns" (Action at page 3), the present sequence, with its well-established medical relevance, has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

As yet another example of utility of the present nucleotide sequence, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not

shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. This is even more true when the genetic locus has been unambiguously linked to human disease (in this particular instance, Wilson's disease).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the Examiner is respectfully reminded that only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (Science, 2001, *291*:1304 *at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not

comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. The PTO has issued numerous patents on polynucleotide sequences that have not been directly shown to be associated "with any diseases or disorder" or useful as "a marker for any disease or condition", the conditions set forth by the Examiner as allegedly necessary to comply with 35 U.S.C. § 101. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,2812 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring in the present Action. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section III below), Applicants submit that the presently claimed polynucleotides must also meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, as well as the reasons set forth in the response to the previous Action, Applicants submit that as the presently claimed nucleic acid molecule has been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-3 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

III. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-3 have been shown to have "a specific, substantial, and credible utility", as detailed in section II above, the present rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants

submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Chernyshev have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

March 16, 2002
Date

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First Named Inventor	Turner, Jr., C. Alexander
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Examiner Name	Chernyshev, Olga
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ENCLOSURES *(check all that apply)*

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- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
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PATENT TRADEMARK OFFICE

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